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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,064	08/02/2005	Pierre Michel Desmons	B45308	4877

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EXAMINER	
GANGLE, BRIAN J	

ART UNIT	PAPER NUMBER
1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,064	DESMONS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6,7,11-14 and 16* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-7, and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/27/2009 has been entered.

The amendment and remarks, filed 1/27/2009, are acknowledged. New claim 16 is added. Claims 1, 6-7, 11-14, and 16 are pending. Claims 11-14 are withdrawn as being drawn to non-elected inventions. Claims 1, 6-7, and 16 are currently under examination.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

It is noted that applicant's arguments are not directed toward any specific rejection. Specific mention is made of Berthet *et al.* in the arguments. However, the letter to the EPO applicant uses to support their arguments of unexpected results and the prior art teaching away refer to reference D1, which is the Granoff *et al.* reference. Therefore, the arguments specifically mentioning Berthet will be addressed with the Berthet rejection, and the arguments based on the letter to the EPO will be addressed with the Granoff rejection.

The rejection of claims 1, 6-7, and newly submitted claim 16, under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That the idea that combining two vaccines into a single multivalent vaccine is obvious leads to the untenable conclusion that any permutation and combination of useful vaccines is obvious under 35 USC 103(a).

2. That the "rationale fails to consider the 2-bleb per se vaccine, specific PorA deficiency in one specific bleb in contradistinction to the lack of PorA deficiency in the second specific bleb."

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, there are three issues with applicant's argument. First, the argument vastly overstates the rationale in attempting to apply it to all vaccines. The examiner has not suggested that all vaccines are obvious. Obviousness is determined based on the facts of each case and a finding that a mixture of known vaccines in the instant case in no way implies that any combination of vaccines is obvious. Second, the rationale used is based on the laws of the United States. It was the Supreme Court that stated that it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. Applicant may find this position untenable, but it is the law. Third, applicant's argument ignores the fact that other motivation for combining the work of Berthet, Vermont, and Baker was discussed. Baker specifically suggested the use of a vaccine that protects against serosubtype P1.7-2,4. The fact that it was specifically suggested that a vaccine for this strain would be useful provides a strong motivation to include it in a multivalent vaccine.

Regarding argument 2, only claim 16 is a "2-bleb vaccine per se." However, Berthet discloses a vaccine containing a mixture of bleb preparations from "2 or more" strains (see page 36, lines 15-19). This is a clear disclosure of a vaccine containing a mixture of blebs from 2 strains. As stated previously, whether or not Berthet disclosed the PorA content of said blebs is immaterial. All that is required to meet the claim limitations is a bleb composition comprising blebs from CU-385 and blebs from strain B:4:P1.7b,4. The reasons behind combining these do not need to be the same as applicant's and there does not need to be any recognition in the prior art that these strains are deficient in PorA or not.

As outlined previously, the instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA, derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA, derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Berthet *et al.* disclose a multivalent vaccine comprising mixtures of meningococcus bleb preparations as well as a pharmaceutically acceptable excipient (see page 36, lines 5-28 and page 33, lines 1-5). Said vaccine comprises mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4 (see page 36, lines 15-19). Said vaccine is also disclosed as comprising any or all of the capsular polysaccharides A, C, Y, or W (see page 36, lines 11-14). Berthet refers to compositions that should be protective against strain CU-385 (page 35, lines 17-30). It is noted that, according to the instant specification, strain CU-385 is deficient in PorA (see page 22, lines 19-22 and page 24, lines 8-11)

Berthet differs from the instant invention in that they do not disclose a composition that comprises blebs from CU-385 in combination with blebs from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Berthet

et al. for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, the multivalent bleb composition against CU-385 is taught by Berthet *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to be useful in protection against meningococcal disease. Therefore, it would have been obvious to combine the two vaccines into a single multivalent vaccine. Finally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because blebs from these strains have been shown to be effective as separate vaccines.

The rejection of claims 1, 6-7, and newly submitted claim 16, under 35 U.S.C. 103(a) as being unpatentable over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002) in view of Vermont *et al.* (Infect. Immun., 70:584-590, 2/2002) and Baker *et al.* (J. Paediatr. Child Health, 37:S13-S19, 2001), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That the rationale fails to consider the unexpected improvement from the prior art, evidenced by the attached letter in the EPO application.

2. That the rationale fails to consider the teaching away from the prior art as evidenced by the attached letter in the EPO application.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding argument 1, applicant's letter to the EPO is noted, however, said letter does not provide any evidence of unexpected results. The data submitted by applicant shows that a vaccine containing blebs from CU-385 and the New Zealand strain induced high antibody titers against both the CU-385 strain and the New Zealand strain. This is hardly unexpected. This is the basic idea behind multivalent vaccines and it is well known that one can broaden coverage of vaccines by including other antigens. The data also show that the combination vaccine against serogroup B induced a much higher antibody titer to serogroup B than the control vaccine, a vaccine that protects only against serogroup C. Again, there is nothing whatsoever unexpected about this result. There is no one of skill in the art who would be surprised to find that a vaccine that only contains serogroup C antigens would not induce a high antibody titer against serogroup B antigens and induced a lower anti-B response than a vaccine containing serogroup B antigens.

Regarding argument 2, despite applicant's assertion, Granoff does not teach away from the instant invention. While sequential administration may be the preferred embodiment, Granoff still discloses a vaccine containing a mixture and specifically states that the outer membrane vesicles can be administered serially *or as a mixture* (page 22, lines 29-30). "The prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed.." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004).

As outlined previously, the instant claims are drawn to a multivalent bleb composition comprising a first bleb composition comprising a first bleb preparation deficient in PorA, derived from the *Neisseria meningitidis* B CU-385 strain and a second bleb preparation that is not deficient in PorA, derived from a *Neisseria meningitidis* B:4:P1.7b,4 strain prevalent in New Zealand.

Granoff *et al.* disclose an outer membrane vesicles (bleb) vaccine that comprises a mixture of blebs from genetically diverse strains of *Neisseria meningitidis* as well as a pharmaceutically acceptable excipient (see page 6, lines 23-31 and page 22, lines 5-20). Granoff *et al.* also disclose a bleb vaccine that contains a mixture of blebs from a serogroup C strain as well as a strain with the serogroup P1.4 (see page 7, lines 19-27). Figure 1 discloses a vaccine with the serosubtype B:4:P1.15, that was used in Cuba and Brazil from 1987-1991. Granoff, on

page 14, refers to an OMV vaccine prepared by the Finley Institute in Cuba which has been given to millions of children in South America. It is clear from an examination of the art and the instant specification, that CU-385 (commonly referred to as the Cuban strain) is the strain referred to in Granoff on page 14 and in Figure 1. Additionally, Granoff *et al.* disclose that the disclosed mixture vaccine has the advantage of broad spectrum protective immunity (see page 15, lines 10-12).

Granoff *et al.* do not explicitly disclose that the bleb vaccine mixture should contain the strain CU-385 and a B:4:P1.7b,4 strain.

Vermont *et al.* disclose an outer membrane vesicle (blebs) vaccine that comprises blebs from a meningococcal strain which has the serosubtype P1.7-2,4 (which is the epidemic serosubtype prevalent in New Zealand) (page 584, column 2, paragraph 1 and page 585, column 1, paragraph 4). As evidenced by Oster (WO 2006/024946, 2006) and Martin *et al.* (Clin. Vacc. Immunol., 13:486-491, 2006), there are different nomenclature systems in use with regard to *Neisseria meningitidis* serosubtypes. According to the different nomenclature systems, serosubtype P1.7-2,4 is the same serosubtype as P1.7b,4.

Baker *et al.* disclose information on the meningococcal disease epidemic in New Zealand. They show that the majority of the strains isolated during the epidemic were B:4:P1.7b,4 (see abstract). Baker *et al.* also suggest that a vaccine that could induce immunity to this strain would be useful in controlling the epidemic (page S18, column 1, paragraph 4).

It would have been obvious to a person of ordinary skill in the art, at the time of invention, to use the bleb preparation from serosubtype P1.7-2,4, as disclosed by Vermont *et al.* in the multivalent bleb vaccine along with a bleb preparation of CU-385 as disclosed by Granoff *et al.* for several reasons. Baker *et al.* state that a vaccine that protects against serosubtype P1.7-2,4 would help to control the New Zealand meningococcus epidemic. In addition, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). In the instant case, a bleb composition against CU-385 is taught by Granoff *et al.* to be useful in protection against meningococcal disease and the vaccine of Vermont *et al.* is taught to

be useful in protection against meningococcal disease. Therefore, it would have been obvious to combine the two vaccines into a single multivalent vaccine. Finally, according to the Supreme Court decision in *KSR International Co. v. Teleflex Inc.*, No. 04-1350 (U.S. Apr. 30, 2007), it would have been obvious to combine elements known in the art by known methods, where in the combination, each element would have performed the same function as it did separately. In this case, vaccines containing blebs from each strain were known in the art, each of these elements would have performed the same function as they would have separately and the results of the combination would have been predictable.

One would have had a reasonable expectation of success because the strains have been shown to be effective as separate vaccines.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571)272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian J Gangle/
Examiner, Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645